Title:.Fungi, Mycotoxins and in situ Breast and Kidney cancers: A water damaged home

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Abstract: **A husband and wife exposed to fungi and mycotoxins in a water-damaged home is presented. The fungi were identified by PCR-DNA tests and tape lift samples that included species of *Aspergillu*s, *Penicillium*, *Eurotium amstelodam*i, and Stachybotrys, among others. ELISA testing for mycotoxins demonstrated aflatoxin, ochratoxin and macrocyclic trichothecenes in HVAC and Room air filters. The husband had aflatoxins (16 ppb) ochratoxin (5.6 ppb) in his urine while the wife was positive for ochratoxin (16.8 [ppb) and trichothecenes (1.14 ppb) in her urine. PCR-DNA test identified *Aspergillus sydowii* in a biopsy of the kidney from the husband. *Penicillium purpurogenum* was identified in a biopsy from the mammary gland from the wife. Pathology of the left kidney and left mammary gland identified *in situ* carcinomas. ELISA tests of the biopsies detected the following mycotoxins as follows: Husband with Hepatitis C (liver – aflatoxin (15 ppb) and kidney ochratoxin and aflatoxin (1.9 ppb) and Wife – breast cancer – ochratoxin (2.5 ppb). The findings are discussed with respect to the role of mycotoxins, fungal fragments and translocation of nano particulates with respect to human health.**

Introduction

Water-damage to Homes, schools and office buildings leads to the proliferation of fungi, Gram negative and positive bacteria. The indoor environment becomes a complex mixture of biocontaminants as a result of this microbial growth (1, 2). The contamination of the indoor air includes MVOCs (3) variety of mycotoxins in airborne fungal fragments smaller than spores (4-5) and in dust from indoor surfaces, carpeting, and ventilation systems samples (6-10), 1, 3-beta D-glucans and endotoxins (11-14), and secondary metabolites of fungi and bacteria (15-17). In addition, air currents mimicking ventilation systems are sufficient to release nano-size (0.03-0.3 microns)

fungal fragments into the indoor environment at a concentration greater than a thousand times the fungal airborne spore counts (18- 21). The aerodynamics of nano particulates in indoor and outdoor air facilitate deposition in the upper and lower respiratory tract. They undergo translocation via the olfactory and trigeminal nerves into the hypothalamus/pituitary axis and the alveolar surfactants into the systemic circulation (22-26). Although human health effects from exposure to the complexity include upper and lower respiratory infections, asthma, fungal sinusitis, sarcoidosis, symptoms of ME/CFS (27-30), little attention has been directed towards indoor mycotoxins and cancer, even though mycotoxins have been detected in sera, urine and tissues of affected individuals(31-38). Aflatoxin B1 is a mutagen and liver carcinogen in humans (39-41). In addition, Ochratoxin A is genotoxic and is associated with urinary tract tumors (42-44). We report in this communication a Husband and Wife exposed in a water-damaged home with mycotoxins in air filters, urine specimens and i*n situ* kidney and mammary carcinomas.

Materials and Methods

Fungi in the Home: The home was originally investigated for the presence of fungi by RestCon Environmental, Sacramento, California. The investigation involved a single tape lift sample, contact ME/Agar plated (RODAC) and nonviable and viable airborne spore count (Allergenco spore strap sampler, 15 liters LPM.fo 75 liters), and wall cavity sampling (Andersen N6 single stage sampler). The results are summarized in Table 2. No attempt was made to determine species of fungi and the detection of mycotoxins.

Home remediation: No report was generated regarding remediation of the home. However**,** there was some plastic used to wall off work areas. Care was not taken that

resulted in carrying ~~f~~ the infected building materials through house to an outdoor dumpster. The affected ceiling in the upstairs bathroom was left open. Recommended remediation practices were not used in the repair and clean up. They lived in the house during and after the repairs and their health issues escalated. They finally moved out to a rental in the summer of 2005, 18 months after the remediation. Post remediation clearance testing was not performed.

Post Remediation Testing: The senior author visually inspected the home on 08/17/07 that revealed the following: The ceiling in the upstairs bath was repaired. The room immediately below had a wall that was not closed. The following samples were taken with sterile rubber gloves as follows: A.C return filter, Inline A.C. filter installed by the manufacturer, dust from the Oreck Vacuum cleaner, intake/ output filters from portable (Flanders) air filtration machines located up stairs and down stairs, along with control filters for the Flanders devices that were in the original packaging. These were placed in zip lock bags, labeled and sent to RealTime Laboratories, Carrollton, Texas for PCR DNA to identify fungal species and ELISA testing for Aflatoxin, Ochratoxin and Macrocyclic trichothecenes as previously published (31-37). The fungal species in environmental samples were identified by RT-QPCR as previously published (38). A portion of the intake HVAC filter was sent to Assured Bio Labs, Oakridge, TN for ERMI-36 fungal identification.

Pathology Reports and Tumor Biopsy Specimens:

Left Breast: The tumor in the left breast was initially identified in a mammogram and needle biopsy. The surgical pathology report was done at UCSF Medical Center. The pathology summary shows nests of ductal cell carcinoma *in situ* with cells that show low

to intermediate grade nuclei in solid and cribiform patterns. Immuno histochemical staining for myoepthelial markers (p63) of smooth muscle confirmed a non-invasive tumor.

Liver Biopsy (Husband): MRI revealed finding suggesting hepatitis. The liver core biopsy was evaluated by Diagnostic Pathology Medical Group, Inc, Sacramento CA. H & E and Trichrome stains reavealed chronic hepatitis consistent with Hepatitis C Grade 1-2, Stage 2 chronicity. However, this diagnosis was made without the knowledge of exposure to mycotoxins present in the water-damaged home, urine and biopsies of the *in situ* tumors.

Kidney Biopsy (Husband): A left kidney mass was identified by MRI during evaluation tor hepatitis The results showed an increasing size of small left renal mass with mid to late phase enhancement. Possible small renal cell carcinoma should be considered. A partial nephrectomy of the mass was performed. Pathology of the mass was done at Mercy San Juan Hospital, Carmichael, CA. The diagnosis was papillary carcinoma, nuclear grade 3, 2.1 cm, margins cannot be assessed.

RealTime Laboratories: Samples of the breasts, liver, and kidney were sent to RealTime laboratories under chain of custody for identification of Aflatoxin, Ochratoxin and Macrocyclic trichothecenes by an ELISA procedure as previously reported (31-36)

Results

Health Histories of Husband and Wife): The health histories with occupation of the home are summarized in **Table 1** as follows:

Husband - bronchitis, rhinosinusitis and sinusitis, chronic fatigue, vertigo (dizziness), loss of balance, Pruiritic skin rash (red sores), neurocognitive deficits (short and long term memory), headaches, cough SOB, and chest pain with inhalation, pneumonia, asthma, allergies, hepatitis C. He has been treated for one Pack per day of cigarettes for 36 years. He was treated for HCV with Daklinza and Sovaldi from February through May 2016. Test for HCV RNA was not detectable at 24 weeks post treatment. He was declared free of Hep C virus.

Wife – pneumonia, chronic fatigue, SOB, wheezing, asthma, memory decline (short and long term), body aches and pain and, Pruiritic skin rash, frontal headaches, left orbital pain, and discoid lupus. One-half pack of cigarettes for 31 years.

Table 1: This table summarizes the symptoms of Husband and Wife that developed and that are persistent after moving into the water-damaged home.

Husband	Wife
Bronchitis, Pneumonia, Rhinosinusitis and Sinusitis, Chronic Fatigue, Vertigo (dizziness), Loss of balance, Pruiritic Skin Rash, Neurocognitive Deficits (short, and long term memory), Headaches, Cough, SOB, Chest Pain with Inhalation, Hepatitis C Virus.	Chronic Fatigue, Maxillary Sinus Congestion, Loss of Balance, Body Aches and Pain, Mental fog, Decreased Memory (short and long term), SOB, Wheezing, Pruiritic Skin Rash, Frontal Headaches, Left Orbital Pain, Mood Instability, Discoid Lupus.

RestCon Results for Fungal Contamination

Table 2 summarizes the major findings of the RestCon evaluation. The RODAC malt extract plates identified *Monila*, *Penicillium*, and *Rhizopus* in the home. The Allergenco

samplers demonstrated total spore counts ranging from 16,320 to 150,820 spores per cubic meter of air. Two different tape lifts samples identified *Stachybotrys* on the floor tiles of the upstairs bathroom before remediation. After remediation a tape lift sample of a discoloration of the hallway wall below the bathroom identified *Stachybotrys* and *Aspergillus/Penicillium*.

Table 2: This table summarizes the results of tests for numbers of viable (cultured) spores per cubic meter of indoor air and percent of total count in four areas of the home. In addition, a tape lift sample from the exposed flooring of the affected bathroom identified *Stachybotrys* at 2+ by microscope observation. The testing was performed by RestCon, Sacramento, CA.

Mold I.D.	**Bdrm Wall N**	**Bdrm Wall N-top**	**Bdrm Wall S**	**Bdrm Top S**
Monila RODAC	1 <1 %	1 <1 %	1 <1 %	1 <1 %
Penicillium - RODAC	370 99 %	200 <1 %	300 99%	100 98 %
Rhizopus RODAC	1 <1 %	200 99 %	1 <1 %	1 <1 %
Total (cfu/m^3) Allergeco	150,820	40,400	80,640	16,320
Tape Lift Samples Before Remediation	Upstairs Bathroom	Stachybotrys 2+		
Downstairs Hallway After Remediation	New Appearance of discoloration on wall below bathroom	Stachybotrys Asp/Pen		

Table 3: This table summarizes the species of fungi identified in the dust samples from the vacuum cleaner and the HVAC filters (Inline and return air). These media were obtained after partial remediation of the home. The most common fungi were

Aspergillus species. *Stachybotrys* was not detected in the filters most likely resulting from the fact that it does not readily shed spores. However, tape lift samples did identify Stachybotrys in two areas of the home (See **Table 2**).

Table 3. Species of Aspergillus and Penicillium detected by PCR-DNA in the filler media and Vacuum Dust. The predominate species are Aspergillus. The return filter to the HVAC system was heavily contaminated.

Vacuum Dust	**Inline HVAC Filter**	**Return Air HVAC Filter ERMI-36 fungal I.D.**
Asp fumigatus *Asp. niger*	*Asp. Fumigatus* *Asp. niger*	*Eur. Amstelodami* *Pen, purpurogenum* *Asp niger* *Paecilomyces variotti* *Pen. Corylophilum* *Wallemia sebi* *Alt. alternata* *Clado. cladosporioides Types 1 & 2* *Clado. Herbarum* *Epicoccum nigrum*

Mycotoxins detected in filter media taken from the home.

Macrocyclic trichothecenes were detected in all filter media as shown in **Table 3**, ranging from 0.38 to 0.966 ppb. The concentration of 0.15 ppb in the room air filter control was negative with respect to the limit of detection. Aflatoxin was positive for all filter media ranging from 1.0 to 5.0 ppb. Ochratoxin was identified in the HVAC filters as follows: Inline (4.5 ppb and return (2.7 ppb). The Flanders room air filter was positive for ochratoxin at 1.4 ppb when compared to the control filter at 0 ppb. Trichothecenes

were also positive at 0.36 ppb in the room air filter. The presence of the mycotoxins in the filter media probably resulted from the release of fungal fragments smaller than spores. The data also demonstrates that the mycotoxins were probably airborne in particulates less than the size of spores.

Table 4. This table summarizes the results of mycotoxins identified in environmental samples taken from the home. The results are in ppb.

Sample	Aflatoxin	Ochratoxin	Trichothecene
Inline filter – HVAC	5.0	4.5	0.966
Return Filter – HVAC	5.0	2.7	0.65
Room Air Filter Flanders	1.0	1.4	0.38
Room Air Filter, Control- Flanders	0	0	0.15

(*Limit of Detection: Ochratoxin– 2 ppb; Aflatoxins– 1 ppb; Macrocyclic trichothecenes– 0.2 ppb*)

Mycotoxins Indentified in the Liver, Kidney and Breast Biopsies and Urine.

The results of the mycotoxins are summarized in **Table 5.** The results for the husband were as follows: Aflatoxin - liver (15 ppb); Kidney (1.9 ppb; urine (16 ppb). Ochratoxin – liver (0 ppb; kidney (9.2 ppb; urine (5.6 ppb). The results for the wife were as follows: Breast – ochratoxin at 2.5 ppb and urine at16.8 ppb. Trichothecenes were not detected in the liver, kidney and breast biopsies while the wife's urine had 1.14 ppb.

Table 5. This table summarizes the mycotoxins in ppb identified in urine and tumor tissue biopsies. The tumors were a renal cell carcinoma and breast ductal cell carcinoma. Both were *in situ* and surgically removed. The liver was biopsied because hepatitis was possibly a result of the Hepatitis C virus. The PCR-DNA tests identified *Aspergillus sydowii* in the kidney biopsy and *Penicillium purpurogenum* in the breast sample (data not shown).

Sample Source	Sex	Aflatoxin	Ochratoxin	Trichothecene
Liver	M	15	0	0
Kidney	M	1.9	9.2	0
Urine	M	16	5.6	0
Urine	F	0	16.8	1.14
Breast	F	0	2.5	0

Discussion

The biocontaminants related to water intrusion and resulting fungal/bacterial growth has been discussed in multiple publication(1-29). Occupants of these environments have been shown in case studies to have health problems such as autoantibodies, asthma, upper and lower respiratory infections, allergies, fungal sinusitis, ME/CFS and sarcoidosis (3, 11, 14, 16, 27-34). In spite of findings that fungal and bacterial fragments are less than the size of spores, little attention has been given to their translocation and health effects via the nasal cavity and surfactants of the alveoli. For example, nano particulates were identified in the olfactory tract and brain of children

exposed to air pollution in Mexico City (25, 26). Even the fact that the pharmaceutical industry is developing intranasal administration of nano-particulates with attached pharmaceuticals should awaken the medical and scientific communities to their role in damage to brain structures (23, 24). When in the alveoli these nano-particles are taken up in the surfactants, transported into the systemic circulation affecting the lymph nodes and systemic organs (44-48).

The fungal species indentified in the three filter media are summarized in Table 4. The species included *Aspergillus fumigatus* and *niger*, in the vacuum dust and inline HVAC filter. The ERMI-36 test of the HVAC intake filter revealed of *Aspergillus niger* and *Penicillium corylophilum* and *purpurogenum* as well as species of other fungi. The differences in the species identified in the three filter media may have resulted from the remediation of the home. The HVAC intake filter had not been changed, thus representing a more accurate identification of fungal species. It is noted that *Stachybotrys* was not identified in any of the filter media. This result may have occurred because *Stachybotrys* does not readily shed spores into the indoor and outdoor air.

The mycotoxins identified in the three filter media are summarized in **Table 5**. The inline HVAC filter installed by the manufacturer had aflatoxins (5.0 ppb), ochratoxin (4.5 ppb), and macrocyclic trichothecenes (0.966 ppb). The intake HVAC filter also had mycotoxins as follows: aflatoxins (5.0 ppb), ochratoxin (2.7 ppb), and trichothecenes (0.65 ppb). Interestingly the Flanders room air filters were positive for aflatoxin, ochratoxin and trichothecenes, while the control filter was negative. Since fungal colonies are fractionated into particulates <one micron by HVAC air currents, it is probable that these mycotoxins, particularly the trichothecenes, represented fungal

fragments less than the size of spores (4, 5, 13, 18-21). In addition, mycotoxins have been identified in dust samples from buildings and carpeting of fungal contaminated homes and buildings (6-10). Thus, the detection of mycotoxins in filter media designed to remove air borne dust should be expected.

The couple was healthy prior to occupation of the home. Shortly after living in the home they developed symptoms and health problems as summarized in **Table 1** These included but not limited to rhinosinusitis, sinusitis, and loss of balance, neurocognitive decline and chronic fatigue. Diagnostic tests revealed hepatitis and left kidney damage in the husband and a lesion in the lefty mammary gland of the wife. Biopsies of the liver and kidney showed hepatitis (probable Hepatitis C) and papillary carcinoma of the kidney. The pathology of the mammary lesion revealed ductal cell carcinoma. PCR DNA tests revealed *Aspergillus sydowii* in the kidney and *Penicillium purpurogenum* in the mammary biopsy. ELISA mycotoxin tests demonstrated aflatoxin in the husband's liver and ochratoxin at 15 ppb and aflatoxin (1.9 ppb) and ochratoxin (9.2 ppb) in the kidney. The mammary lesion was positive for ochratoxin at 2.5 ppb. In addition, the urine samples were positive for mycotoxins as follows: Husband (ochratoxin at 5.6 ppb); and the wife had ochratoxin at 16.5 ppb and trichothecenes at 1.14 ppb. In conclusion, the presence of mycotoxins in the filter media, liver, kidney and breast biopsies demonstrated exposure to mycotoxins and the uptake into the liver and breast. Aflatoxin and ochratoxin are mutagenic and carcinogenic in animals and humans (39-43, Moreover, the role of fine and nano particulates released from fungal colonies needs further assessment with respect to distribution to organs and health of the animals and humans exposed in water-damaged indoor environments (18-37, 33-36. 44-49). It

should be noted that although the mycotoxins are identified in materials from water-damaged buildings, the fungus producing the mycotoxins may not have been identified during sampling thus missing fungal species (50). Even though the husband was positive for Hepatic C Virus, the resulting hepatitis may have been either additive or synergistic interaction with mycotoxins (51-54). Finally, the detection of aflatoxins and ochratoxin in the *in situ* cancers of the kidney and mammary gland is consistent with the mutagenic and carcinogenic properties of these mycotoxins (39-44). Thus, it appears from the observations that greater attention must be directed towards the airborne mycotoxins as observed in the room and HVAC filters shown in Table 4. Perhaps, the airborne mycotoxins present in fungal fragments less than the size of conidia have a role in the health of occupants of water-damaged indoor environments (1-27).

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